CLINICAL PROCEEDINGS

of the

CHILDREN'S HOSPITAL

WASHINGTON, D. C.

MAY 9 1955

April 1954

VOLUME X NUMBER 4

on every count Superior vitamin supplements for infants

- **Superior flavor** — Exceptionally pleasant "taste-tested" blend of flavors carefully protected during manufacture . . . no unpleasant aftertaste . . . readily accepted without coaxing.
- **Superior stability** — Outstanding stability is achieved by Mead's specially developed solution. Poly-Vi-Sol and Tri-Vi-Sol require no refrigeration . . . no expiration dates on labels—and may be safely autoclaved with the formula.
- **Superior miscibility** — Both disperse instantly in formula, fruit juice or water . . . mix easily with Pablum® cereal and other foods.
- **Superior convenience** — Light, free-flowing . . . no mixing necessary . . . calibrated droppers assure easy, accurate dosage. For infants, drop directly into the mouth. For children, measure into a spoon.
- **Superior hypoallergenicity** — Poly-Vi-Sol® and Tri-Vi-Sol® supply crystalline vitamins in a completely hypoallergenic solution.

Poly-Vi-Sol

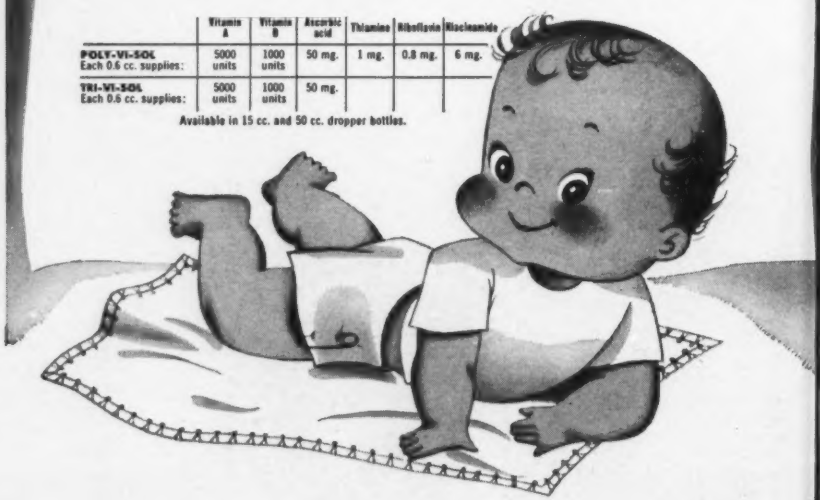
SIX ESSENTIAL VITAMINS FOR DROP DOSAGE

Tri-Vi-Sol

VITAMINS A, D AND C FOR DROP DOSAGE

	Vitamin A	Vitamin D	Ascorbic acid	Thiamine	Riboflavin	Niacinamide
POLY-VI-SOL Each 0.6 cc. supplies:	5000 units	1000 units	50 mg.	1 mg.	0.8 mg.	6 mg.
TRI-VI-SOL Each 0.6 cc. supplies:	5000 units	1000 units	50 mg.			

Available in 15 cc. and 50 cc. dropper bottles.



MEAD JOHNSON & COMPANY · EVANSVILLE, INDIANA, U.S.A. MEAD

MEAD, JOHNSON & COMPANY, Suite 419 Eig Building, 8641 Coleville Road, Silver Spring, Maryland. JU 9-1222

CLINICAL PROCEEDINGS

OF THE CHILDREN'S HOSPITAL

13th and W Streets, Washington 9, D. C.

Vol. X *April 1954* No. 4

CONTENTS

LETTERER-SIWE'S DISEASE. *Dr. Joseph Lopresti, Dr. Jerome Bernstein* 65

DIVERTICULUM OF THE ILEUM SIMULATING A TUMOR. *Dr. J. Ogle Warfield, Dr. Preston McLendon, Dr. Paul Adkins* 74

CONTROL OF HYPERTENSION IN ACUTE GLOMERULONEPHRITIS. *Dr. Arthur Goodrich* 77

CLINICO PATHOLOGICAL CONFERENCE. *Dr. E. Clarence Rice, Dr. Jerome Bernstein, Dr. Gordon McDonald* 83

EDITOR-IN-CHIEF
E. CLARENCE RICE, M.D.

MANAGING EDITORS
FREDERIC G. BURKE, M.D. SIDNEY ROSS, M.D.
JOSEPH M. LOPRESTI, M.D.

ASSOCIATE EDITORS
JOHN P. McGOVERN, M.D. DAVID A. ST. MARTIN, M.D.
ROBERT H. PARROTT, M.D. MARSHALL C. SANFORD, M.D.
IRVING E. HALL, JR., M.D. ROBERT B. SULLIVAN, M.D.

GENERAL MANAGER
SUE BARRON EMMERSON

Contributing Editors from the Resident Staff: JOHN D. BUNCE, M.D.; BELINDA C. STRAIGHT, M.D.; JEAN D. LOCKHART, M.D.; MILTON S. GLATT, M.D.; H. E. C. MILLAR, M.D.; ARTHUR L. GOODRICH, M.D.; ALLYN B. GIFFIN, M.D.; AND ARDWIN H. BARSANTI, M.D.; JEROME BERNSTEIN, M.D.; ROGER BERGSTROM, M.D.

Publications Committee of the Medical Staff: E. CLARENCE RICE, M.D.; THOMAS BRADLEY, M.D.; FREDERIC G. BURKE, M.D.; PRESTON A. MCLENDON, M.D.; ROBERT H. PARROTT, M.D.; SIDNEY ROSS, M.D.; HAROLD STEVENS, M.D., AND JOHN A. WASHINGTON, M.D.

PUBLISHED MONTHLY BY THE STAFF AND RESEARCH FOUNDATION OF THE CHILDREN'S HOSPITAL, WASHINGTON, D. C.

Cases are selected from the weekly conferences held each Sunday morning at 11:00 A.M., from the Clinicopathological conferences held every other Tuesday afternoon at 1:00 P.M., and from the monthly Staff meeting.

This bulletin is printed for the benefit of the present and former members of the Attending and Resident Staffs, and the clinical clerks of Georgetown and George Washington Universities.

Subscription rate is $2.00 per year. Those interested make checks payable to "Clinical Proceedings Dept.," The Children's Hospital, Washington, D. C. Please notify on change of address.

Copyright 1954, Children's Hospital

Entered as second class matter November 21, 1946 at the post office at Washington, D. C., under the Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 538, Act of February 28, 1925, authorized January 17, 1947.

LETTERER-SIWE'S DISEASE

Joseph LoPresti, M.D.
Jerome Bernstein, M.D.

CASE PRESENTATION

This 13 month old white female* was apparently in good health until one week prior to admission when she developed bilateral cervical swelling and difficulty in feeding, but no elevation of temperature. This was diagnosed as mumps and no specific therapy was given.

Three days prior to admission the patient developed bilateral otitis media and pharyngitis. This was treated with penicillin. In spite of this therapy a bloody, purulent discharge from the ears developed. The bilateral cervical swelling increased slightly and the patient was admitted to the hospital.

The infant was a full term delivery, weighing 3.4 kgm. at birth. At delivery the cord was wrapped around the infant's neck and she was kept in oxygen for three days. She was followed by a pediatrician periodically and immunizations were complete. She was treated for eczema of the scalp since the age of four months.

The family history was non-contributory.

Physical examination on admission revealed a well-developed, well-nourished, 13 month old white female who appeared very irritable but in no acute distress. The temperature was normal. There was a petechial rash over the face, scalp, abdomen, and low back. There was a small occipital hematoma, a result of head banging. The throat was moderately injected. The external canals of both ears were very red and the tympanic membranes were moderately inflamed. The lungs were clear to percussion and auscultation. The heart rhythm was normal and there were no murmurs. The liver edge was palpated one centimeter below the costal margin and spleen was not palpable. The neurological examination revealed no abnormalities. There was marked bilateral cervical and submandibular lymphadenopathy. Axillary, supraclavicular, and inguinal adenopathy was slight.

Urinalysis revealed one to two white cells per high powered field. Hemoglobin was 10.6 gm., hematocrit 37 per cent, white blood cells 11,100 segs. 55, bands 7, lymphocytes 28, monocytes 1, and eosinophiles 9. The platelets were normal.

Diagnosis on admission was bilateral otitis media, cervical adenitis and pharyngitis.

The patient was placed on antibiotics with no improvement. Ear cultures grew E. coli which was moderately sensitive to chloromycetin and aureomycin.

After one week in the hospital, the patient developed a fever, the rash became more widespread over the anterior and posterior thorax and head. The cervical and submaxillary nodes enlarged slowly. The liver became larger and the spleen was questionably palpable. X-ray of the chest revealed infiltration throughout both lung fields. The report read that this might be bronchopneumonia but miliary tuberculosis should be considered. At this time there were still no pulmonary changes on physical examination.

The spinal fluid was normal except for low chlorides. NPN was 30 mg. per cent, total protein 3.5 gm. with albumin 2.4 gm. and globulin 1.1 gm. Prothrombin time was

---

* From the service of Dr. Robert Martin.

normal. Skin tests for tuberculosis and histoplasmosis were negative. Bone marrow examination revealed erythroid and myeloid hyperplasia. No abnormal cells were seen. The only change in the hemogram was an increase in the white cell count.

After 10 days the patient became lethargic and she developed an intermittent fever. The liver and lymph nodes were larger and a purpuric rash appeared over the abdomen. It was felt by several observers at this time that this represented Letterer-Siwe's disease, tuberculosis or histoplasmosis.

Physical examination on the 15th hospital day revealed a hemorrhagic rash over the head and abdomen, pitting edema of the lower extremities, external strabismus, course rales throughout both lung fields, liver edge four finger breadths below the costal margin, and cervical, suboccipital, posterior auricular, axillary, and inguinal adenopathy. The spleen was not palpable.

Seventeen days after admission a lymph node biopsy was performed in the left cervical region. The patient's condition continued to deteriorate and she died on the 18 hospital day.

A postmortem examination revealed a one year old white female weighing 8.9 kilograms and measuring 79.0 cm. in length. The skin over the scalp, face, anterior and posterior thorax, and abdomen was covered with petechiae, many of which had become papular. The external canals of both ears were markedly inflamed. The cervical lymph nodes were markedly enlarged bilaterally.

On section there was a marked amount of mediastinal emphysema. The anterior and posterior mediastinal and axillary lymph nodes were markedly enlarged and dark purple. The mesenteric lymph nodes were markedly enlarged and light purple in color (Fig. I & II).

Gross Examination of Organs: The lungs were light purple and showed a marked amount of emphysema in the periphery. There were many light gray cysts [measuring 0.1 to 0.3 cm. in diameter] scattered over the superior and lateral surfaces of the lungs. The cut surface showed a marked amount of pale yellowish infiltration and many

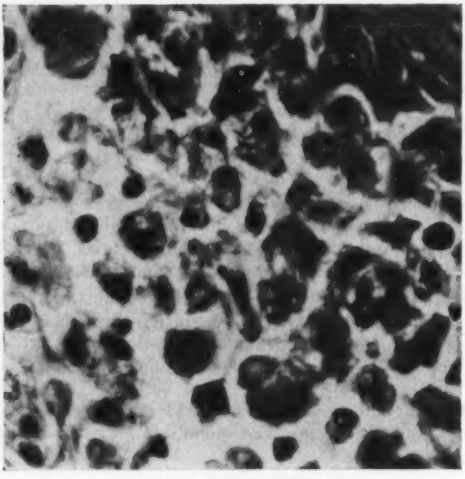


FIG. I. Lymph Node

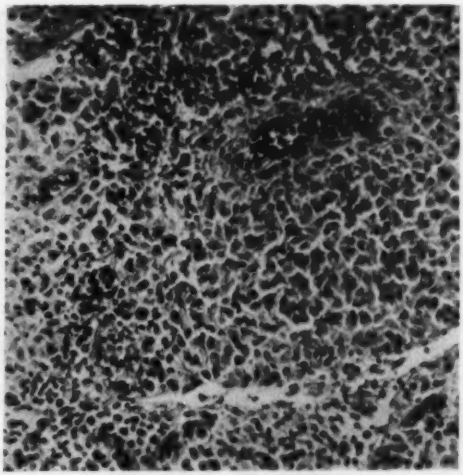


FIG. II. Lymph Node

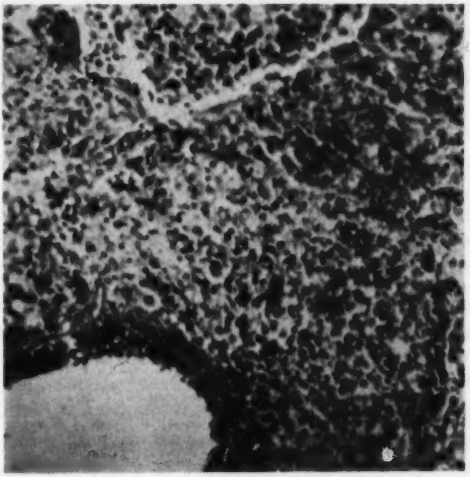


FIG. III. Lung

small, scattered cysts, particularly in the superior portions. The peri-bronchial and mediastinal lymph nodes were moderately enlarged and dark purple. The lungs were approximately two and one half times the average weight for the age (Fig. III & IV).

The liver was approximately twice the average size for the age, very smooth and very firm. The spleen was three times the average weight for the age and was firm

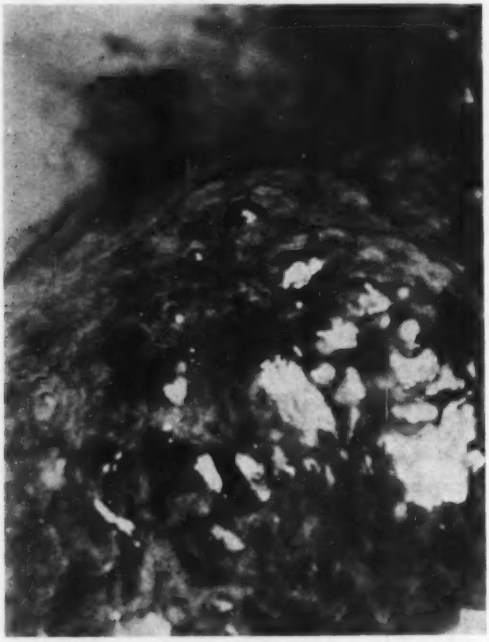


FIG. IV. Lung

and dark purple. The cut surface was dark purple with a marked amount of light purple infiltration scattered evenly throughout the organ.

The right ureter was dilated to approximately twice the normal size. At the right uretero-vesicular junction there was a marked constriction. Gross examination of the brain revealed a normal external contour, but marked congestion throughout. Near the occipito-parietal junction there was a large collection of venous channels suggesting a hemangioma. Coronal sections showed uniform congestion. The following organs showed no evidence of gross abnormalities: thyroid, thymus, heart, pancreas, adrenals, and kidneys.

Microscopic Examination: There was practically no normal looking lung tissue present. The alveoli and most of the bronchioles and blood vessels were completely filled with histiocytes, polymorphonuclear leukocytes, and very large reticulo-endothelial cells. The reticulo-endothelial cells were very large and varied in shape from oval to polygonal. The cytoplasm was generally light pink. The nuclei varied in shape from circular to eliptical or bean-shaped. Some of the cells were multinucleated. The nuclei varied from dark staining to mere outlines. Many of the reticulo-endothelial cells appeared to contain a fatty material. There were many cyst-like areas spread evenly throughout the section showing no specific lining. There were many large phagocytic cells which gave a positive Prussian blue reaction.

The muscle fibers of the heart were moderately separated due to congestion and edema. The liver showed marked fatty degeneration. There was a moderate infiltra-

tion of the large reticulo-endothelial cells in the hepatic trinities, particularly around the bile ducts. The blood vessels were moderately dilated, and there was a slight increase in the amount of connective tissue. There was a very small amount of iron pigment.

The spleen showed marked congestion and hemorrhage. There was a moderate patchy infiltration of the reticulo-endothelial cells and a reduction in the number of lymphocytes. The pancreas showed slight congestion and slight hyalinization of the connective tissue. The cells of the islets of Langerhans stained very poorly. Throughout the gastro-intestinal tract there was a moderate infiltration of the reticulo-endothelial cells, particularly in the submucosal regions.

The adrenal glands showed a moderate medullary and cortical degeneration with some fatty metamorphosis. This involved, particularly, the zona fasciculata and the zona glomerulosa. There was slight medullary congestion. Most of the glomerular tufts of the kidneys were enlarged and practically filled the entire Bowman's capsule. The cells of the tubules showed marked swelling and very indistinct boundaries. The lumens of most of the tubules were filled with a pink staining granular material.

The architecture of the lymph nodes was completely distorted by the marked infiltration of the large reticulo-endothelial cells. The lymphocytes were markedly reduced in number. There were some areas of necrosis of the reticulo-endothelio cells which was represented by pink staining homogeneous material. A special stain for fat revealed the presence of a moderate amount in many of the cells.

Histopathological Diagnosis: 1) Reticulo-endotheliosis (Letterer-Siwe disease); 2) Fatty metamorphosis of the liver and adrenals; 3) Fatty infiltration of the renal tubules.

DISCUSSION

Dr. Joseph LoPresti

The term reticulo-endotheliosis is a general one used to define a group of little understood diseases which include eosinophilic granuloma, Hand-Christian-Schuller, Letterer-Siwe's, Gaucher's, Neimann-Pick's, and Tay-Sach's diseases. These clinical entities occur sporadically and infrequently in the pediatric age group. A specific etiology has not been determined for any of these conditions, a feature common to all of them is the involvement of the reticulo-endothelial system. In some, there is an associated accumulation of a specific lipoid in various organs of the body. A strong racial, familial or hereditary tendency often is present. This group of interesting diseases is important because of the differential diagnosis and the serious prognostic implications which they present. In all types of reticulo-endothelioses the roentgen appearance of the skeletal system when it is involved is identical. The lesions present themselves as translucent shadows or shadows of decreased density which are cast by the granulomatous, hyperplastic reticulo-endothelial cells. When the long bones are involved there may be internal erosion of the cortex which may result in a pathological fracture of the bone. The differential diagnosis of reticulo-endothelioses is made by pathological and chemical determinations. The infrequency with which one of these diseases is encountered in pediatrics is illus-

trated by an analysis of the records of Children's Hospital, Washington, D. C. Only 14 cases could be located and of these there were 9 males and 5 females. Of more significance was the racial distribution which showed 12 white and only 2 colored patients. This suggests that these diseases are more common in the white than in the colored race.

Eosinophilic granuloma, Hand-Christian-Schuller disease, and Letterer-Siwe's disease are considered under the large heading of eosinophilic xanthomatous granulomata. A clearer understanding of the inter-relationship of these three disease entities has evolved. This fact has aided greatly in their classification and understanding. Farber, Thanhauser, Holm, Walgren, and Green have advanced the concept that there are four phases in the development of eosinophilic xanthomatous granuloma: 1) a proliferative phase in which histiocytic proliferation with accumulation of eosinophilic leukocytes is observed. In this phase, there is no evidence of foam cells. 2) A granulomatous phase with increase of blood vessels and fibrils, reticulo-endothelial cells and histiocytes, eosinophils, and incipient lipoid accumulation in macrophages. 3) A xanthomatous phase with nests and isolated foam cells and 4) A fibrous phase considered as a healing stage. These four phases often show no definite line of demarcation. During the course of the disease the histiological features may overlap considerably. It is evident from histologic studies that the solitary eosinophilic granuloma is the "monosymptomatic, early stage of the systemic disease." However, Jaffe, Lichtenstein, and Otani believe that eosinophilic granuloma is a virus granuloma distinct from the other diseases.

In eosinophilic granuloma, the patients are usually unaware of their bone lesions. In the beginning they do not complain of bone pain. The lesion may be found accidentally by x-ray examination. Later, a dull ache is experienced, especially if the lesion is near a joint. It is during this painful stage that the bone lesions usually are discovered. The roentgenograms reveal osteolytic lesions with ill defined borders. These skeletal defects usually are single but may be multiple and do not possess a dense zone at their peripheries. The location of the lesion is not characteristic and they may be found in any part of the osseous system. The skull, pelvis and the upper portions of the femora frequently are involved. One of our cases, particularly, is interesting, because it illustrates the inter-relationship of these diseases.

This was a five year old white female admitted to the Children's Hospital in 1945 with a pathological fracture of the left humerus. Biopsied material was reported as histiologically characteristic of eosinophilic granuloma. The next year this patient developed chronic mastoiditis with drainage from the right ear. Osteolytic lesions were found in the skull, ribs, clavicles and pelvis. A mastoidectomy was performed

and the material studied microscopically. The pathologist's report at this time was Hand-Christian-Schuller disease. X-ray therapy to the skeletal lesions was instituted and a seven year follow-up revealed an asymptomatic completely recovered patient.

Hand-Christian-Schuller disease occurs most commonly in infants and children of the white race, and is more common in males than in females. The historical triad of exophthalmos, diabetes insipidus and defects in membranous bones is not invariably present. Xanthomatous skin lesions may occur. A generalized form of the disease with involvement of the lungs, lymph nodes, spleen and liver has been described. The appearance of foam cells and an increase in cholesterol content of the tissues is diagnostic of the xanthomatous phase of this disorder. However, the blood cholesterol levels are normal. The skeletal lesions predominate. In the skeletal system the radiolucent, granulomatous proliferations replace the radio-opaque bone and appear roentgenographically as areas of diminished density. These lesions are found usually in the skull, pelvis, scapulae, ribs and extremities. Involvement distal to the elbows and the knees occurs infrequently. These bone defects may be single or multiple, usually rounded, and of variable size. The lesions do not have a dense zone at their peripheries and again the appearance of the bone lesions produced by the different reticulo-endothelioses is the same on the roentgenogram. When the tubular bones are involved, internal erosion of the cortex may cause a pathological fracture of the bone. The differential diagnosis of the reticulo-endothelioses is made pathologically and chemically not roentgenographically.

Letterer-Siwe's disease is the earliest and most acute form of eosinophilic xanthomatous granuloma. It occurs primarily in infants and clinically is characterized by fever, progressive anemia, hemorrhage, hepato-splenomegaly, outstanding enlargement of the lymph nodes and a rapidly fatal course. The outstanding histological feature is reticulo-endothelial proliferation with little or no cellular lipoid accumulation. The absence or paucity of lipoid accumulation and the lack of the development of granulomatous tissue is due to the rapidly fatal course of this disease. When it occurs a little later in life, the progress is slower and the skeletal system becomes involved. The cranium is involved very often as it is in Hand-Christian-Schuller disease. The roentgenographic findings are identical with those found in eosinophilic granuloma and Hand-Christian-Schuller disease. Four of our patients had Letterer-Siwe's disease. Two were white and two were colored and all were under fifteen months of age. Two of the patients demonstrated lesions in the skull and one, a two month old colored male, showed multiple osseous lesions on x-ray examination. After admission to the hospital, the courses were febrile and progressively downhill despite all therapeutic methods. In all instances the diagnosis was

confirmed at autopsy. Recent reports indicate that some cases of Letterer-Siwe's disease respond to aureomycin and suggest an infectious etiology.

The generalized form of eosinophilic xanthomatous granuloma occurring in infants (Letterer-Siwe's disease) is usually a fatal disease. The prognosis is entirely different if the first symptoms become manifest later in life. The older the patient the more favorable is the prognosis. If the disease remains confined to the skin and osseous system or even to the classical triad of Hand-Christian-Schuller's disease, the prognosis is not too unfavorable. The generalization of this disease with involvements of lungs, liver and spleen immediately changes the prognosis in infancy as well as in later life. Sosman and others have shown that x-ray therapy of the bone lesions, especially of the membranous bones and skull has been successful in some cases. The same holds true for x-ray therapy of enlarged lymph nodes. No success has been noted in similar therapy of skin and visceral lesions.

The second category of the reticulo-endothelioses may be termed "lipid" and includes Gaucher's, Neimann-Pick's and Tay-Sach's diseases. This group possesses a number of common features. 1) The etiology is unknown. 2) There appears to be strong racial, familial and hereditary tendencies. 3) There is an accumulation in the reticulo-endothelial system of abnormal amounts of a specific lipid characteristic for each entity. 4) Central nervous system symptoms are present in all. 5) There is a uniformly unfavorable outcome.

In Gaucher's disease the specific lipid which accumulates in the tissues is cerebroside (kerasin). The disease occurs in infantile and adult form. It is much rarer in infancy than in adulthood. The infantile form is acute and invariably fatal. The pathognomonic feature is the presence of a unique, large pale cell (the Gaucher's cell) in the spleen, lymph nodes, liver and bone marrow. There appears to be a marked familial tendency present in the recorded cases. Clinically, the disease is characterized by retarded physical and mental development. The spleen enlarges and as the disease progresses, the liver also enlarges. The extremities become flexed and rigid. Dysphagia, trismus, laryngeal spasm, and spells of cyanosis occur. Blindness and deafness appear and the child increasingly becomes mentally debilitated. Fever with pulmonary involvement and death during a spell of cyanosis terminates the course of the disease. The duration is about two to six months. While bone lesions may occur in Gaucher's disease, the cranium is rarely affected in contrast to the eosinophilic xanthomatous granuloma where the cranium is affected frequently. However, in Gaucher's disease the vertabrae are involved more commonly than in the other reticulo-endothelioses. The one case of acute infantile Gaucher's disease in this series was a three month old white male who died at six months of age. An x-ray survey of the skeletal system was normal. The diagnosis was proven by chemical analysis of the liver and spleen.

In Neimann-Pick's disease the characteristic specific lipoid is sphingomyelin (lecithin). In contrast to Gaucher's disease, this condition is more common in children than in adults. A familial and racial tendency is present. The unstained Neimann-Pick's cell has a characteristic vacuolated, foamy appearance entirely different from the opaque, large, pale Gaucher's cell. The clinical features are hepato-splenomegaly, generalized adenopathy, diffuse pigmentation of the skin, patchy blue-black spots on the mucous membranes of the mouth, digestive disturbances, physical and mental deterioration, slight hypotonicity, emaciation of the extremities, mongoloid facial expression, and extreme cachexia. These patients may have a cherry red spot in the macula lutea.

Because of similarity of the nervous and retinal changes, some authorities have felt that Tay-Sach's disease was a partial manifestation of Neimann-Pick's disease. However, Klenk isolated a new lipoid from the brain in Tay-Sach's disease which he named ganglioside and thus established a chemical difference between the two disease entities. When bone involvement occurs in this disease as in Gaucher's disease, the cranium is rarely, if ever affected.

In Tay-Sach's disease the specific lipoid which accumulates in tissues is ganglioside. Clinically, there is a history of the development of weakness with gradual loss of muscular power and failing vision in a previously healthy and normal baby, usually of Jewish parentage. As the disease progresses, mental retardation develops. The presence of a cherry red spot on examination of the fundus is of pathognomonic significance. On the other hand, even in the abscence of the cherry red spot, the finding of optic atrophy or of other retinal changes in a child with both idiocy and blindness makes the diagnosis of Tay-Sach's disease a good possibility. Decerebrate rigidity develops and death ensues from marasmus or an intercurrent infection, after an average duration of illness of 18 months or by the time the infant is two years of age. Microscopically, universal changes are observed throughout the entire nervous system. The ganglion cells are swollen and assume varied globular shapes and the dendrites are enlarged and balloon-like in appearance. An associated destruction of cortical myelinated fibers also is present. As in the other lipid reticulo-endothelioses, bone involvement when it occurs, spares the cranium. Of the three children with Tay-Sach's disease in this series one was of non-Jewish antecedents, a very rare occurrence in this particular disease entity.

There is no specific treatment for the lipid reticulo-endothelioses. In the pediatric age group, the outcome invariably is fatal. In Gaucher's as well as in Neimann-Pick's diseases when the splenomegaly reaches tremendous proportions, splenectomy is performed to relieve pressure.

From a roentgen point of view, the differential diagnosis of the reticulo-endothelioses involves those diseases which may produce similar changes

in the osseous system. These include the metastatic malignant lesions such as the neuroblastomas, sympathicoblastomas, and myelomas; infectious diseases such as lues, and osteomyelitis; cysts and solitary bone lesions such as the epidermoidomas.

In conclusion, the salient clinical, histological, and roentgen features of the reticulo-endothelioses have been presented. A short discussion of the differential diagnosis, prognosis and treatment has been mentioned. From the point of view of the radiologist, any or all of these diseases may produce changes in the skeletal system which are similar and indistinguishable one from the other. The final diagnosis can be established only by pathological and chemical studies. In general roentgen therapy of the skeletal lesions is beneficial, particularly in eosinophilic granuloma and Hand-Christian-Schuller disease. With the exception of eosinophilic granulomas the outcome usually is poor when generalized visceral involvement occurs.

DIVERTICULUM OF THE ILEUM SIMULATING A TUMOR

J. Ogle Warfield, M.D.
Preston McLendon, M.D.
Paul C. Adkins, M.D.

CASE REPORT

R. S., a seven year old white male, was admitted to the Children's Hospital on June 16, 1953 because of the presence of blood in the stool, anemia and abdominal pain. Two and one half months prior to admission, the patient began complaining of intermittent abdominal pain, and during the course of investigation, it was found that he was anemic. He was placed on iron and vitamins with a satisfactory response. Five weeks later he had another episode of abdominal pain and passed dark blood with a stool. The iron and vitamins were discontinued and the patient was well until two days prior to admission, when he again had cramping abdominal pain without localization, vomited and passed tarry stools. The vomitus contained no blood. Family history and past history were essentially negative.

Physical examination on admission revealed a rather pale, well developed, well nourished white male of about seven. No gross abnormalities were found. The abdomen was soft, no masses were palpable. Laboratory: Hemoglobin 4.8 gms. erythrocytes 1,900,000; leukocytes 29,400; differential: segmented 56, bands 2, eosinophiles 14, lymphocytes 27, monocytes 1. There was marked hypochromia and anisocytosis. At proctoscopic examination much wine colored blood was obtained and no abnormalities were noted up to a distance of eight inches.

The child was transfused with 600 ml. of whole blood on the day of admission and on June 18th repeat blood studies showed a hemoglobin of 8.8 gms., erythrocytes 2,600,000 and a normal differential white cell count. Tourniquet test was negative. For the first three days after admission the child had small amounts of blood in the stool, and thereafter, the stools were free of gross blood. He received an additional trans-

fusion of 400 ml. of whole blood. Barium enema and upper gastro-intestinal x-ray series were performed and no abnormalities were noted. The patient was discharged on June 24th asymptomatic, to be followed by his pediatrician.

The child was readmitted to Children's Hospital on February 4, 1954 because of continued episodes of melena and intermittent vague abdominal pains. Physical examination again was not remarkable; the skin appeared to be of good color. Laboratory studies revealed a hemoglobin of 9.0 gms., hematocrit 34 per cent, leukocytes 16,400 with normal differential. Preoperative diagnosis was a bleeding Meckel's diverticulum.

On February 5th, an exploratory laporotomy was performed under nembutal-ethylene-curare anesthesia. The abdomen was entered through a right rectus incision. At a distance of approximately 30 cm. from the ileocecal valve, a firm mass, approximately 3 x 2.5 cm. in size was encountered. This mass occupied the mesenteric side of the bowel and extended into the mesentery. It was rounded, firm, smooth and the serosa overlying it was slightly injected. The lumen of the terminal ileum distal to this mass was noted to be full of blood, whereas the bowel proximal to it was empty. The mesentery supplying this area contained many firm markedly enlarged lymph nodes, some 5–6 cm. in diameter. These nodes extended down toward the root of the mesentery. It was the clinical impression that we were dealing with a tumor of the small bowel, and on this premise it was decided to do a wide resection of the bowel and accompanying mesentery. Accordingly, a 42 cm. segment of ileum, including the tumor, mesentery and most of the enlarged nodes was resected and an end-to-end anastomosis was performed. The patient had an essentially uneventful postoperative course, and was discharged from the hospital on his seventh postoperative day.

Pathological report of the specimen by Dr. E. Clarence Rice was as follows: The specimen consists of a 42 cm. segment of small intestine. At its midportion is a diverticulum which measures 2 cm. in internal depth and extends into the mesentery. It is lined by what appears to be intestinal mucosa. There is a hemorrhagic area at the junction of the mucosa of the gut and the diverticulum which measures 4 mm. in diameter. Microscopic Examination: The diverticulum is lined by intestinal mucosa. A hemorrhagic and ulcerated area showing considerable connective tissue at the base with leukocytic infiltration of the wall is noted. The lymph node shows an increase in connective tissue. Pathological diagnosis was: (1) Diverticulitis with ulceration, (2) Lymphadenitis, chronic.

DISCUSSION

Diverticula of the small intestine are not uncommon. Meckel's diverticulum, the most common, represents a persistence of the proximal portion of the vitelline duct, and is found in 2–3 per cent of adults. The vagaries of this minor anomaly are well known. The great majority of diverticula are asymptomatic and are found incidentally at laparotomy or at autopsy. However, pathological complications may arise, particularly from a Meckel's diverticulum. According to Gross[1], the most common manifestation is gastro-intestinal bleeding, which was present in this case. Other symptoms which may arise are abdominal pain, inflammation, intussusception starting with the diverticulum, and, rarely, volvulus and infarction of the diverticulum if the neck is narrow. If the remnant of the primitive yolk stalk persists as an attachment between the diverticulum

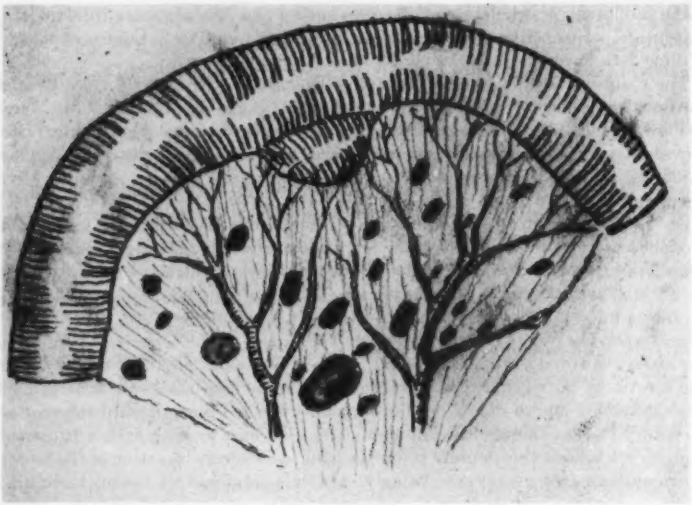


FIG. 1

and the umbilicus, complications such as an umbilical fistula, cyst inside the umbilicus or obstruction from the band may occur.

According to Christine[2], a Meckel's diverticulum occurs on the antimesenteric side of the bowel anywhere from 15 to 90 cm. from the ileocecal valve. Gross[1] states "Rarely the diverticulum swings over against the mesentery and acquires a filmy covering which gives it the appearance of having an intramesenteric portion." In this case, the diverticulum actually arose on the mesenteric border of the ileum and the communication with the bowel was on that side. (Fig. 1) It is quite possible that the structure was more closely related to a form of duplication of the small bowel, with a communication with the lumen of the ileum, than to the classical Meckel's diverticulum. Duplications of the bowel are found most frequently in the ileum[1] and frequently lie within the mesentery. They may or may not connect with the alimentary canal. Embryologically they are of different origin than a Meckel's diverticulum and probably represent a persistence of a vacuole which may appear during the transition of the gut from the solid to the cystic state (fifth to twelfth week)[3, 4]. Hemorrhage may also occur in a duplication as a result of ulceration of the mucosa.

Regardless of the etiology of this diverticulum, the location on the mesenteric border, combined with its consistency as a result of inflammatory reaction, made it closely simulate a tumor of the small bowel. The enlarged mesenteric nodes served to further this impression. Frozen section of the

mass at the time of operation might have made differentiation possible and a less extensive resection might have been carried out. On the other hand, whatever the pathological diagnosis, resection of the bowel with end-to-end anastomosis was felt to be the treatment of choice of this mass.

SUMMARY

A case of a seven year old boy with persistent vague abdominal pain and gastro-intestinal bleeding is presented. At laparotomy a firm mass on the mesenteric side of the distal ileum was found with greatly enlarged lymph nodes. Grossly at operation this resembled a tumor of the small bowel with local metastases and was treated as such. Pathologically, the mass was a diverticulum with ulceration and inflammation.

BIBLIOGRAPHY

1. Gross, R. E.: The Surgery of Infancy and Childhood. Saunders, Philadelphia.
2. Christine, A.: Am. J. Dis. Child., **42:** 544, 1931.
3. Bremer, J. L.: Arch. Path., **38:** 132, 1944.
4. Arey: Developmental Anatomy, 4th Ed., Saunders, Philadelphia.

CONTROL OF HYPERTENSION IN ACUTE GLOMERULONEPHRITIS

Arthur Goodrich, M.D.

The control of hypertension in acute glomerulonephritis may pose a difficult problem. This case is presented as one which illustrates this problem and its management.

Ideally an agent for the control of the hypertension encountered in some cases of acute glomerulonephritis should be one which 1) relieves general vasospasm, 2) lowers blood pressure 3) improves renal function and 4) is free from toxic effects, especially cardiac and renal ones. No product is available which fulfills all of these criteria.

The oldest and most effective therapeutic agent now in use is magnesium sulfate and although it has been used for thirty years, there is still some debate as to the optimal route of its administration. It may be ineffectual if administered orally. Blackfan[9] claimed that good results could be obtained if a 50 per cent solution in a dosage of 30 to 60 cubic milliliters is given orally three times a day. This mode of therapy may be effective if it is instituted early at the first sign of hypertension. The results depend on the fact that the magnesium ion is excreted poorly in the early oliguric phase of acute nephritis. Intravenous therapy is effective and can be controlled if administered carefully and slowly with frequent blood pressure

recordings. The usual concentration is a 2 per cent solution and the average dose is 100 to 150 cubic milliliters. However, the danger of toxicity is present. Intravenous medication should be reserved for patients with severe encephalopathy. Magnesium sulfate is usually given intramuscularly. Other agents such as Priscoline, Apresoline, veratrum viride derivatives, and hexamethonium have been useful in the control of hypertension in adults. Lack of familiarity with the use of these products in children was one of the reasons which prompted the writing of this paper.

CASE PRESENTATION

H. J., an eight year old negro female was admitted to the Children's Hospital of the D. C. on October 9, 1953 because of generalized convulsive seizures which occurred shortly before hospitalization. The present illness began one week prior to admission with frontal headaches and intermittent nose bleeds which persisted. Swelling of the face was also noted at this time. For the preceding four days she had periumbilical pain and on the night before admission she vomited several times.

The patient has had no previous serious illnesses or convulsive episodes. There is no pertinent family history.

Physical examination showed a well developed, well nourished colored female who was semi-comatose and acutely ill. The face was slightly swollen. Blood pressure was 170/120 in both arms. There was mild injection of both tympanic membranes and of the throat. There was dried blood in the nose. The lungs were clear. Auscultation of the heart disclosed a soft apical systolic murmur and a suggestion of a gallop rhythm. Liver and spleen were not palpable. There was a definite left facial paralysis, and a questionable weakness of the left arm. Reflexes were decreased or absent in the lower extremities but present in the upper extremities. The eye grounds were normal.

A lumbar puncture was done immediately, the fluid being obtained under a pressure of 300 milliliters of water, and contained 11 lymphocytes, 130 milligrams per 100 milliliters of protein and 77 milligrams of sugar. Two grains of phenobarbital had been given prior to the lumbar puncture. Following this she became alert; and the facial paralysis and left arm weakness disappeared. Hemogram showed hemoglobin 10.0 grams, 19,600 leukocytes with 89 per cent polymorphonuclears. The serum urea nitrogen was 31 mg./100 ml. The initial urine contained 1 gm./100 ml. of albumin, 3+ acetone, many hyaline casts, but only 3–5 leukocytes and 0–1 erythrocytes per high power field.

Magnesium sulfate was given intramuscularly in doses of 6.0 milliliters of 50 per cent solution (3 grams) every eight hours, and small amounts of fluid were given by mouth. On the first day her fluid intake was only 400 milliliters and her output, only 220 milliliters. There was no evidence of cardiac failure. On November 10, 1953, her fluid intake was somewhat better, though there was some vomiting. Despite the continued intramuscular administration of magnesium sulfate, the patient's blood pressure remained high, averaging 140/110. Clinically she was more alert and seemed to be better. On this day the urine contained 10–20 erythrocytes and 100 mgm. of albumin. On November 11th she was still oliguric and the blood pressure was elevated to 180/130. The buttocks were hard from the frequent intramuscular injections. An intravenous dose of 2.5 grams of magnesium sulfate in a 25 per cent solution was given and was followed by a slight, transient fall in blood pressure.

Although her urinary output increased greatly and the serum urea nitrogen was

14 mgm., on the fourth hospital day, the blood pressure reached a new high of 210/130 during that afternoon. It was decided to give the intravenous administration of magnesium sulfate a further trial and a five per cent solution was given by a slow drip. Eleven hours later the blood pressure was down to 128/90 and magnesium sulfate was discontinued, the blood pressure rising five hours later to 140/110. The drug was again administered and after one hour the blood pressure was down to 128/90 and the drug discontinued. She had received a total of 12.5 grams of magnesium sulfate. Blood pressure stabilized around 120/70. On the sixth hospital day, a slight pitting edema of the legs was noted and the liver extended 4 centimeters below the ribs. The next day this had disappeared. She continued to do well clinically.

A chest x-ray on the eighth hospital day disclosed the cardiac silhouette to be markedly widened to the left, with some increase in bronchovascular markings bilaterally. On the seventeenth day (October 25), the cardiac shadow had receded almost to normal limits. On October 31, the heart was reported to be slightly dilated on x-ray examination. An intravenous pyelogram done on October 30 was normal. Electrocardiograms done on October 19 and 31 showed low flat T waves in lead 1 and the chest leads. Sedimentation rate on October 21 was 42 milliliters per hour (Wintrobe). On October 23, the urine had returned to normal. PSP test done on October 22 showed only 20 per cent excretion in ½ hour, 98 per cent in five hours. She was discharged on October 31 in good condition to receive modified bed rest, low salt diet and was to be followed in the out-patient medical clinic.

DISCUSSION

The treatment of this particular patient and reports from the literature on the use of various agents for the control of hypertension in acute glomerulonephritis will be discussed.

This patient showed the following major manifestations of acute glomerulonephritis.

1. Encephalopathy
2. Hypertension
3. Oliguria
4. Transient and slight edema
5. Symptoms of cardiac failure: These did not appear until the fifth hospital day, after the patient had received a large amount of magnesium sulfate intravenously. It is not clear whether these symptoms occurred in the natural course of the disease, or whether they may have been the result of magnesium sulfate toxicity.

The symptoms of encephalopathy in this patient cleared spontaneously after lumbar puncture and the administration of phenobarbital, before any magnesium sulfate had been given. However, the drug is known to be very effective in relieving the symptoms of encephalopathy. This may be due to the general effect in relieving vasospasm.

Magnesium sulfate was administered intramuscularly to relieve hypertension but it was not very effective. Only after large amounts had been given intravenously was a fall in blood pressure sustained.

This patient showed symptoms of mild cardiac failure on the fifth hospital day, after other major symptoms had been cleared. Cardiac failure in acute nephritis is associated usually with hypertension.[8] It has been reported that magnesium sulfate has a toxic effect on the myocardium. The patient was not digitalized because the symptoms were mild and transient and were not present during the acute stage. Burke and Ross[5] reported that cardiac failure was the principal cause of death in acute glomerulonephritis, and advised digitalization in all patients who showed any signs of cardiac failure other than mere cardiac enlargement. In view of this, perhaps it would have been wise to have digitalized the patient.

Magnesium sulfate is the oldest therapeutic agent in use for combating the hypertension in acute glomerulonephritis, and it is still the treatment of choice. The usual route of administration is the intramuscular one. Harris and De Maria[6] have reported more effective results with intravenous magnesium sulfate with no increase in toxicity.

Renal function in children with acute glomerulonephritis has been studied by Harris[6], Etteldorf[2], and Rapaport[3]. In acute glomerulonephritis all the tests of kidney function are somewhat reduced. The glomerular filtration rate was found to be definitely reduced by all observers. The renal blood flow was found to be impaired by the majority of observers. The tubular excretion as measured by the para-amino hippurate excretion test also was slightly reduced. There was some improvement in renal function after 1–3 weeks; but, generally, renal function remained depressed after the urine findings returned to normal.

The studies performed to determine the effect of magnesium sulfate on renal function in normal children showed no change according to Harris[6]. Etteldorf[4] reported tubular excretion to be increased significantly but no other significant changes were noted.

In contrast, studies reporting on the effect of magnesium sulfate on renal function in children with acute glomerulonephritis showed the glomerular filtration rate and the renal blood flow to be increased.

The principal toxic manifestations of the magnesium ion are 1. A cutaneous vasodilation expressed as a feeling of warmth, 2. Depression of respiration, and 3. Possible depression of myocardial function. The margin between an effective dose and a toxic dose is often small.

It is believed that magnesium sulfate produces its effect by the ability of the magnesium ion to relieve general arteriolar spasm[2, 3, 6]. The early relief of symptoms of encephalopathy is attributed to this. Whether magnesium has a particular effect in relieving renal arteriolar spasm is not clear. Its beneficial effect on renal function is thought to be due to a rise in perfusion pressure through the glomeruli with a concomitant falling systemic blood pressure.

This probably is due to the increased glomerular filtration rate. Harris[6] reported that a level of 5 mgm./100 ml. in the blood was necessary for a beneficial effect, using the parenteral route of administration.

Priscoline produces hypertension by causing neurogenic afferent arteriolar constriction. This results in a fall in renal blood flow which is undesirable in acute glomerulonephritis. Hexamethonium is a very potent chemical substance. It is an autonomic blocking agent and produces undesirable side effects. It causes urinary retention, constipation and renal damage. Patients with renal disease usually do not do well when treated with hexamethonium. Royce[8] reported the use of veriloid in six patients with hypertension and acute glomerulonephritis with good results. Veratrum derivatives have been used extensively for the control of hypertension in adults but its use in children has been limited. Royce reported an initial decrease in renal blood flow and urine output followed quickly by an increase to normal. No comment was made of the effect on other renal functions. Toxic manifestations are hypertension, shock, bradycardia, and cardiac irregularities. Antidotes which should be available are adrenalin for the hypertension and atropine for the bradycardia. Veriloid may be given by the oral, intramuscular, or intravenous routes; but is most effective intravenously. The method used in this study was first to observe the patient for 2–12 hours. Then if the blood pressure was 160/100 or higher, Veriloid was given intravenously and was discontinued if the blood pressure fell. Veriloid is a general vasodilator, acting through the central nervous system, and also acts as a renal vasodilator. It increases cardiac output, causes bradycardia, and reverses the strain pattern on the E.K.G. Good results were obtained in six patients with moderately severe hypertension.

The author bases his claim of superiority of Veriloid over magnesium sulfate to the beneficial effects of the former on the myocardium and states that magnesium sulfate has a deleterious effect on the heart and cardiac function. This latter statement is not substantiated.

In this patient we gave a 5 per cent solution of magnesium sulfate by a slow intravenous drip until the blood pressure approached normal. A blood pressure of less than 140/100 was considered an adequate criterion for stopping the drug. When hypertension recurred the intravenous administration was resumed and continued until the blood pressure again returned to normal. Calcium chloride was kept in a syringe at the bedside to combat toxic reactions but none occurred. The child received a total of 250 ml. of this 5 per cent solution, or 12.5 gm. of magnesium sulfate over a period of 12 hours, before a permanent fall in blood pressure occurred.

Magnesium sulfate was used because it is the therapeutic agent which has produced the most successful results. Harris and De Maria[6] indicate that it is safe and more effective via the intravenous route. The report on

apresoline by Rapaport[7] was interpreted as being unfavorable. The quoted reference[8] on the use of Veriloid in children cannot be interpreted as a basis for routinely establishing this therapeutic regime, but in view of the excellent results obtained in adults, more work with its utilization in children should be performed. Investigations as to its effect on renal function in children with acute glomerular nephritis are needed.

Magnesium sulfate proved to be a valuable therapeutic agent in the treatment of our patient. A beneficial effect was not obtained until a 5 per cent solution was administered intravenously. Our choice in the future would be a 2 per cent solution. The intravenous route should be reserved for patients with severe encephalopathy or those who do not respond to the oral or intramuscular administration of a 50 per cent solution. When the parenteral routes are utilized frequent blood pressure readings should be obtained and the patient observed carefully for the toxic effects of magnesium, i.e.; central nervous system depression. An antidote of 5–10 ml. of a 5 per cent solution of calcium chloride or calcium gluconate should be kept at the bedside and administered intravenously if toxic symptoms occur.

BIBLIOGRAPHY

1. Hebert: Acute Glomerulonephritis in Childhood, J. Ped. **40:** 549, 1952.
2. Etteldorf and Tuttle: The Effects of Magnesium Sulfate on Renal Function in Children with Acute Glomerulonephritis, J. Ped. **41:** 524, 1952.
3. Rapaport et al: Renal Function Studies in Acute Glomerulonephritis in Children. J. Ped. **41:** 823, 1952.
4. Etteldorf et al: Renal Function Studies in Pediatrics II, Ama. J. of Dis. of Children, **83:** 301, 1952.
5. Burke and Ross: Acute Glomerulonephritis, A review of 90 cases. Clin. Pro. of the Children's Hospital, **3:** 83, 1947.
6. Harris and De Maria: Effects of Magnesium Sulfate on Renal Dynamics in Acute Glomerulonephritis in Children. Pediatrics **11:** 191, March, 1953.
7. McCrory and Rapaport: Effects of Apresoline in Children with Acute Nephritis. Pediatrics **12:** 29, July 1953.
8. Royce: Hypertensive Phase of Acute Nephritis, Pediatrics, **12:** 358, Oct. 1953.
9. Blackfan, K. D., Mills, C. A.: Effect of two per cent Magnesium Sulfate Solution on Cerebral Symptoms. Tr. An. Pediat. Soc. **35:** 197, 1923.

CLINICAL-PATHOLOGICAL CONFERENCE

Directed By: E. Clarence Rice, M.D.
Assisted By: Jerome Bernstein, M.D.
By Invitation: Dr. Gordon R. Mac Donald*

This 4 months old colored male was admitted to Children's Hospital on October 1, 1949 and died on October 17, 1949.

The baby had been apparently well until the day prior to admission at which time he developed fever, vomited all feedings, and had five brown semisolid stools. He was brought to the out-patient department, where weak tea was prescribed and a blood count was done. The symptoms continued and on the following day the infant was admitted for treatment and observation because of severe anemia.

This patient was the second born of premature twins of a seven months gestation, weighing 1 pound 9 ounces and 2 pounds respectively. The first twin died of pulmonary atelectasis after seven hours. The patient remained at Freedman's Hospital for 2 months and was discharged weighing 5 pounds. He did well on an evaporated milk formula and pureed foods at home, and was not seen by a physician after that.

On admission to the Children's Hospital the patient's temperature was 102°F. Examination revealed a fairly well nourished but undeveloped colored male infant weighing 10 pounds. There was loss of skin turgor, pretibial edema and marked pallor of the conjunctivae and mucous membranes.

During the first three hospital days the patient's temperature varied from 99°F. to 101°F. and thereafter was normal. The initial hemogram revealed 2 million erythrocytes, 5.5 gms. of hemoglobin. On October 2, the child was transfused with 100 ml. of whole blood. The following day, he had six loose brown stools and appeared anemic and dehydrated. On October 4, marked pallor, scrotal and lower extremity edema were noted. At this time abdominal palpation revealed a large firm mass in each flank, and examination of the urine revealed gross hematuria which persisted throughout the remainder of his hospital stay. A flat film of the abdomen taken at this time was interpreted as "Hepatosplenomegaly with displacement of the large and small gas distended bowel forward and toward the midline by bilateral flank masses." Pallor persisted, hemoglobin was 3.2 gms. and the patient was transfused again. Dyspnea developed on October 6 and oxygen was started and continued. On October 7 bright red blood was noted in the stools and for the remainder of the patient's hospital stay the stools were black, semisolid, small in volume, and occurred two to three times daily. Dependent edema progressed and he retained very little of the feedings taken by mouth. Fluid and electrolytic balance was maintained by intravenous infusions and clysis. Despite adequate intake of fluid, the patient became anuric on the 13th and remained so till his demise four days later. On the 17th the patient developed severe dyspnea, cyanosis, had clonic convulsions and died.

Treatment while in the hospital consisted of blood transfusions, parenteral fluids, oxygen, penicillin, and other supportive measures.

Significant laboratory data:

1. Erythrocytes 1.1 million to 2.5 million; hemoglobin—3.2 gms. to 8.0 gms.; leukocytes—15,000 to 30,000 with 60-80% polymorphonuclears.

2. Bone marrow—"Decreased megakaryocytes, otherwise normal."

---

* Attending Urologist, Garfield Memorial Hospital.

3. Sickling preparation—negative.
4. Coombs test and abnormal A or B agglutinins—negative.
5. Fragility test—patient's cells: hemolysis begins—0.38%; hemolysis complete—0.28%; control: hemolysis begins—0.46%; hemolysis complete—0.34%.
6. Kahn and Mazzini—negative.
7. Prothrombin time—108% of normal.
8. Non-protein nitrogen—October 4, 42 mgm./100 ml.; October 12, 148 mgm./100 ml.; October 14, 123 mgm./100 ml.; October 16, 126 mgm./100 ml.
9. Total protein 4.94 gms./100 ml.; Albumin 3.92 gms./100 ml.; globulin 1.02 gms./100 ml.
10. Urinalyses—gross or microscopic blood in all specimens; albumin 10–400 mgms./100 ml.
11. Stool culture—no pathogens found.

DISCUSSION

Dr. Gordon Mac Donald.

In brief, the protocol is that of a four month old premature colored male whose clinical course is characterized by progressive azotemia, eventual anuria and death.

As concerns the role of infection, there is little supporting evidence as recorded in this protocol. The dehydration noted on admission could explain the temperature elevation at that time. It is stated that the temperature was normal throughout the illness after the third hospital day. All urine specimens contained red blood cells and albumin, but in none were any plus cells noted. The absence of pyuria makes pyelonephritis very unlikely.

Since the progressive renal failure implies bilateral disease, renal neoplasm may be given little consideration.

Congenital anomalies of the urinary tract must be strongly considered. Lower urinary tract obstructions, such as urethral valves or contracted vesicle neck, usually take longer to cause renal failure. This is because the bladder acts as a temporary buffer in preventing upper urinary tract damage. The higher the level of obstruction the earlier renal failure will be manifested. Bilateral uretero-pelvic obstructions cannot be ruled out in this case. Polycystic disease also should be strongly considered. Bilateral flank masses were noted on the plain x-ray. These masses, most likely renal, were described as large and firm on physical examination, but no comment was made as to contour or irregularity.

Dr. Bernstein mentioned the possibility of venacaval obstruction above the level of the renal veins. That possibility cannot be ruled out. The scrotal and lower extremity edema mentioned on October 4 is consistent. However, it is rather hazardous to reach that conclusion from the protocol as presented here, particularly if you are considering a fulminating bilateral pyelonephritis as the major factor.

In conclusion, I feel there is not sufficient evidence for supporting bilateral renal infection as the primary problem. I would favor a congenital bilateral obstruction of the upper urinary tract.

PATHOLOGICAL DISCUSSION

Dr. Jerome Bernstein.

At postmortem examination the abdomen was found to be markedly protuberant and there was considerable edema of the external genitalia. The lower lobes of both lungs contained dark purple depressed areas and there was moderate edema throughout. Microscopic examination showed atelectasis and emphysema. The other significant findings were confined to the brain and kidneys and their vascular supply.

The inferior vena cava distal to the liver was thrombosed and distended as were both renal veins. The arterial supply was unaffected. Both kidneys were approximately four times their usual size and their surfaces were yellow-green in color. The right kidney showed superficial hemorrhages. The capsules stripped with some resistance and the cut surfaces showed poor differentiation between cortices and medullae.

Microscopically, both kidneys showed massive venous thrombosis with evidence of infarction, this being more marked adjacent to the pelvis. Organization of some of the infarcted areas had taken place. Polymorphonuclear leukocytes and round cells were present in the thrombosed vessels and had invaded the parenchyma. A number of the tubules showed marked degeneration, some with calcific deposits. Innumerable bacilli were present. In the cortical areas vague remnants of the glomeruli and tubules could be discerned in an otherwise amorphous tissue. Many polymorphonuclear leukocytes were present. Those glomeruli close to the capsule were more distinct and there was hemorrhage within the Bowman's capsule. One area beneath the renal capsule was the site of an abscess.

The brain was smaller than normal. The Rolandic veins over the right hemisphere to a point midway in the parietal lobe were thrombosed, and those on the left were thrombosed as far as the Sylvian fissure. Several thrombosed veins entered the longitudinal sinus. An excess of fluid was present in the arachnoid spaces. The frontal gyri were irregular and small. Section disclosed a hemorrhage in the white matter of the posterior portion of the right parietal lobe measuring 7 x 3 x 3 cm. Another small hemorrhage was present in the midportion of this lobe.

Postmortem cultures: 1. Cisternal fluid—*E. coli*; 2. Heart's blood—*Proteus morganii*; 3. Kidney—*E. coli*.

Pathological diagnosis: Bilateral renal infarction and thrombosis of renal veins and inferior vena cava. Thrombosis of meningeal veins. Cerebral

hemorrhage. Pulmonary edema, atelectasis and emphysema. Uremia (clinical).

Dr. E. Clarence Rice.

Thrombosis of the renal veins has not been a common necropsy finding, nor has occlusive disease in the young been seen with any frequency. Generally such findings have been associated with diarrhea and ileocolitis and less commonly with certain contagious diseases, skin infections and cellulitis. Most of the patients have been three months of age or younger.

Campbell states that the process may start with infarction and thrombosis of the parenchymal vessels, beginning in the glomeruli, or it may extend from a phlebitis involving the vena cava, ureteral, ovarian, spermatic, suprarenal or accessory renal vessels or the renal vascular pedicle. It is probable that in most cases the infarction follows venous thrombosis which extends up to and involves the kidney. Both kidneys are affected in about half of the patients. Campbell states that the entire kidney is usually involved, but only a portion of the organ may be damaged.

Allen states that in adults thrombosis of the main renal vein generally produces hemorrhagic infarction, but gives the clinical picture of the nephrotic syndrome with hypertension. He finds that adults whose kidneys are so involved show comparatively few renal changes in contrast to the marked changes observed in children. The reason for this disparity may be due to the difference in the collateral circulation available.

An awareness of the possibility of such a condition being present in a baby and the possibility that surgical intervention may save the patient's life should be in the minds of physicians who are called to see children who have apparent or evident pain in the loin with hematuria associated with diarrhea, cellulitis of the thigh or a phlebitis. Vomiting, constipation, anuria and fever with increasing debility may be seen. Edema of the lower extremities may be a part of the picture. The urine will show albumin, blood and probably casts and pus. An intravenous pyelogram will usually give valuable aid in making the diagnosis. When this condition is recognized, early immediate removal of the kidney, if but one kidney is affected, may be life saving.

REFERENCES

Campbell, Meredith: Clinical Pediatric Urology, Philadelphia, W. B. Saunders Co., 1951.

Regan, F. C., and Crabtree, E. G.: Renal Infarction, Clinical and Surgical Entity, J. Urol. **59**: 981–1013.

Allen, Arthur C.: The Kidney, New York, Grune and Stratton, 1951.